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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/620,559	07/17/2003	Dan Peters	2815-0224P	9251

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EXAMINER

HUANG, EVELYN MEI

ART UNIT	PAPER NUMBER
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1625

DATE MAILED: 01/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/620,559

Applicant(s)

PETERS ET AL.

Examiner

Evelyn Huang

Art Unit

1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 15-23 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 15-23 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

1. Claims 15-23 are pending. Claims 1-14 have been canceled according to the preliminary amendment.

Priority

2. The instant is a divisional of 09/450637, issued as 6645977.

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification of in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 19 is for treating a disease responsive to the activity of nicotinic acetylcholine receptor modulators. A modulator may be an agonist, an antagonist, or a partial agonist etc. The binding assay described in the disclosure does not distinguish between agonist and antagonist. There is no indication as to whether the compound would act as an agonist (useful for treating the diseases requiring an agonist), or as an antagonists (useful for treating diseases susceptible to an antagonist). The rejection is applicable to claims dependent on claim 19.

Art Unit: 1625

Claim Rejections - 35 USC § 112(1)

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15, 17-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. R1 as 2-(3-methoxymethyl) as recited in claim 15 is not described in the specification.

Claim Rejections - 35 USC § 112(1)

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention. The following evaluation factors have been considered.

- a. *Nature of the invention.*

The instant invention is drawn to an azabicyclo-[3.2.1] octene compound for use as a modulator of nicotinic acetylcholine receptor in the treatment of a disease responsive to the activity of a nicotinic acetylcholine receptor modulator. The diseases are recited on pages 5-6 of the specification..

- b. *State of the prior art and the level of the skilled in the art.*

Art Unit: 1625

3-substituted azabicyclo-[3.2.1] octene compounds similar to the instant are known to be inhibitors of monoamine reuptake (Moldt, WO 97/13770, PTO-1449) and are employed as intermediates in the preparation of the corresponding azabicyclo-[3.2.1] octanes (Archer, 3133073, PTO-1449, column 2, compound III; Lu, 5731317, PTO-1449, column 17, compound 14).

It is well recognized in the art that affinities for nicotinic receptors do not differentiate agonists from antagonists, which are known to elicit different effects on disease conditions mediated by the nicotinic receptors. For example, nicotinic antagonists such as mecamylamine impair working memory function, while nicotinic agonist treatment may improve attention, learning and memory and nicotinic antagonist treatment can cause deficits (Levin, Psychopharmacology 1998, 138(3-4): 217-30, submitted by Applicant). At present, the correlation between receptor binding of the ligand and its effect on the various diseases in vivo has not been established.

The level of the skilled in the nicotinic acetylcholine receptor art is high.

c. *Predictability/unpredictability in the art.*

The high degree of unpredictability is well recognized in the nicotinic acetylcholine receptor art. A slight modification of the compound would lead to profound changes in its biological activity as evidenced in the very different K_b values exhibited by structurally similar compounds (Olesen, WO 97/11072, PTO-1449, page 12, Table 1).

d. *Amount of guidance/working examples.*

The preparation of the example compounds has been described.

The procedures for the in vitro nicotinic acetylcholine receptor binding assays are described and the results shown for the example compounds on page 17 of the specification. No functional assays or in vivo procedures are described.

e. *The breadth of the claims.*

Applicant's assertion that all the inventive compounds are effective modulators (i.e. agonists, antagonists, partial agonists and allosteric modulators as defined on page 5 of the specification) useful for treatment of any disease responsive to the activity of a nicotinic acetylcholine receptor modulator does not commensurate with the scope of the objective enablement, especially in view of the high degree of unpredictability in the art, the lack of

Art Unit: 1625

correlation between in vitro receptor binding and the effect on the diseases in a human or an animal, and the absence of guidance as to which compounds are agonists, antagonists, partial agonists or allosteric modulators (paragraphs c, d above).

f. *Amount of undue experimentation.*

Since insufficient teaching and guidance are provided by the specification (paragraphs c-d above), one of ordinary skill in the art, even with high degree of skill, would not be able to use the compounds as claimed without undue experimentation.

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. While this application claims to be the divisional of 09/450637 (issued as 6645977), a restriction requirement has not been made in the parent application 09/450637.

Claims 15-23 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6645977. Although the conflicting claims are not identical, they are not patentably distinct from each other. The 3-thienyl or 2-thienyl of instant R1 is described in the small genus of claim 1 and further recited in the species claim 3 of the patent. The last compound wherein R1 is 3-bromobenzothienyl of instant claim 16 is recited in claim 3 of the patent (third compound to the last). The method of use in the patent is encompassed by the instant method claims.

Art Unit: 1625

8. Claims 15-23 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 18-20 of copending Application No. 10/380653. Although the conflicting claims are not identical, they are not patentably distinct from each other. The nicotinic receptor agonist benzothienyl compound of the copending claims has a 8-H or 8-ethyl whereas the compound of the instant claim 16 has a 8-methyl as R. However, H, methyl and ethyl are optional choices (claims 18-19 of 10/380653, definition of R). One of ordinary skill in the art therefore would be motivated to replace the copending H or ethyl with the homologous methyl to arrive at the instant invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

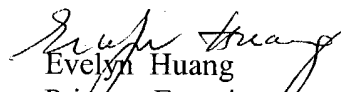
9. No claims are allowed.

Audia (6107307) discloses a 3-bicyclic heteroaryl-8-azabicyclo-[3.2.1]-oct-2-enes for inhibition of serotonin reuptake. However, Audia is not prior art since it was filed on 6-7-1999, claiming the benefit of provisional application 60/089951, filed on 6-19-1998, which is after the instant priority date of 5-28-1998.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 571-272-0686. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Alan Rotman can be reached on 703-308-4698. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.


Evelyn Huang
Primary Examiner
Art Unit 1625